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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* NORBERT BEIER, WOLFGANG SCHOLZ, ULRICH BETZ, and MARIAN BRAENDLE

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Appeal 2016-000194
Application 12/991,524[1]
Technology Center 1600

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Before JEFFREY N. FREDMAN, ELIZABETH A. LAVIER, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

LAVIER, *Administrative Patent Judge*.

## DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellants seek review of the Examiner's rejections of claims 8, 14–16, 18, 20, 22–24, 26, and 28. We have jurisdiction under 35 U.S.C. § 6(b). For the reasons set forth below, we AFFIRM.

## BACKGROUND

The Specification describes "the use of 2-Methyl-4,5-di-(methylsulfonyl)-benzoyl-guanidine, or derivatives thereof, for the

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[1] Appellants state the real party in interest is Merck Patent GmbH. Appeal Br. 1.

enhancement of insulin sensitivity and the preservation or increase of β-cell compensation," as well as "for the prophylaxis and therapy of Type II diabetes mellitus, the Metabolic syndrome, diabetic nephropathy and/or neuropathy." Spec. 1, ll. 6–11. Claim 8 is illustrative:

> 8. A method for the treatment of a disease that is associated with β-cell dysfunction, comprising administering to a patient an effective amount of 2-methyl-4,5-di(methylsulfonyl)-benzoyl-guanidine, and/or a physiologically acceptable salt and/or solvate thereof, such that the β-cell dysfunction in the patient is decreased.

Appeal Br. 17 (Claims Appendix).

## REJECTION MAINTAINED ON APPEAL

Claims 8, 14–16, 18, 20, 22–24, 26, and 28 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gericke,[2] Tracey,[3] Patti,[4] and Siffert.[5] Ans. 2–3.

## FINDINGS OF FACT

The Examiner's findings, which we adopt as our own, are set forth on pages 6–10 of the Final Rejection. We highlight the following for context.

2-Methyl-4,5-di-(methylsulfonyl)-benzoyl-guanidine, also known as "rimeporide," was known in the art at the time of the claimed invention. *See*

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[2] Gericke et al., US 6,673,968 B1, issued Jan. 6, 2004.
[3] Tracey et al., US 2003/0212104 A1, published Nov. 13, 2003.
[4] Patti et al., *Coordinated Reduction of Genes of Oxidative Metabolism in Humans with Insulin Resistance and Diabetes: Potential Role of* PGC1 *and* NRF1, 100 PNAS 8466 (2003).
[5] Siffert & Düsing, *$Na^+/H^+$ Exchange in Hypertension and in Diabetes Mellitus – Facts and Hypotheses*, 91 BASIC RES. CARDIOL. 179 (1996).

Gericke 1:6–13; *see also* Appeal Br. 3–4; Final Action 7. Rimeporide is part of a class of compounds, sulfonylbenzolguanidines, useful as therapeutic agents. *See* Gericke 1:18–47. As is especially relevant to the Examiner's findings, Gericke includes "diabetes and late complications of diabetes" among the conditions that can be treated with this class of compounds. Gericke 1:41–42; *see also* Final Action 7.

As the Examiner notes, Gericke "does not specifically teach the treatment of a disease that is associated with β-cell dysfunction." Final Action 7. However, the Examiner finds that Tracey describes treatment of insulin resistance (which was known to be associated with β-cell dysfunction (*see* Patti Abstract)) and type II diabetes using NHE-1[6] inhibitors that are "highly homologous" to the compounds of Gericke. Final Action 7–8 (citing Tracey Abstract, ¶ 193). Also, the Examiner cites Patti as disclosing that insulin resistance "precedes and predicts the development of type II diabetes mellitus," which is "characterized by insulin resistance and pancreatic β-cell dysfunction." *Id.* at 8 (citing Patti Abstract, 8466). Finally, the Examiner relies on Siffert as teaching that NHE-1 "plays a pivotal role in a variety of cardiovascular pathologies," including diabetic nephropathy, a complication that may be suffered by 30–40% of patients with type I or type II diabetes. *Id.* (citing Siffert 180, 186).

The Examiner finds that one of ordinary skill in the art would have been motivated to combine the references because Gericke teaches that rimeporide "is useful for the treatment of diabetes, in general, and it would have been obvious to one of ordinary skill in the art to apply the general

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[6] Sodium-hydrogen exchanger type (or isoform) 1. *See* Final Action 7–8.

teaching of the treatment of diabetes to the two specific subtypes of diabetes, including type II diabetes." Final Action 9. The other cited references provide, *inter alia*, the connections between type II diabetes and insulin resistance with β-cell dysfunction. *See id.* at 9.

## DISCUSSION

Appellants argue the pending claims in three groups.[7]

### *A. Claims 8, 14–16, 18, 20, and 24*

Appellants' central argument is that the prior art references do not teach or suggest that rimeporide "would decrease beta-cell dysfunction and/or preserve or increase β-cell compensation." Appeal Br. 5; *see also id.* at 3 (emphasizing the "functional interaction between the particular drug and the particular condition of beta-cells"), 8–11. In support, Appellants maintain that Gericke's "generic" recitation of various applications of rimeporide (including diabetes) do not amount to a disclosure of "any particular use." *Id.* at 4 (discussing Gericke 1:14–47); *see also id.* at 8. Further, Appellants assert that "different types of diabetes can be treated using different functional means," such that "[f]or example, a suggestion in a reference that a compound may be useful to treat type II diabetes does not necessarily suggest a method wherein type II diabetes is treated in a way

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[7] Appellants do not include claims 26 and 28 in any of these groups, or otherwise address them specifically. However, claims 26 and 28 appear in Appellants' list of Claims on Appeal (*see* Appeal Br. 2) and the Claims Appendix (*see id.* at 17–18). Claim 26 depends from claim 8; claim 28 depends from claim 24. *See id.* Accordingly, we treat claims 26 and 28 as standing or falling with claims 8 and 24.

'such that the β-cell dysfunction in the patient is decreased.'" *Id.* at 5–6. Indeed, according to Appellants, "Gericke and Tracey teach the effect of NHE-1 inhibition . . . which is based on treating insulin resistance" (*id.* at 8) and that the prior art in fact "teaches away from an enhanced NHE-1 activity as a target for β-cell dysfunction therapy, and thus away from the claimed invention" (*id.* at 11). Accordingly, Appellants assert that Gericke and Tracey focus on improving the insulin sensitivity of cells in peripheral tissues/organs, rather than on combatting dysfunction of β-cells in the pancreas. *See id.* at 8–9. Siffert further supports this lack of "connection between NHE-1 inhibition and the ability to decrease β-cell dysfunction" in the cited art, Appellants maintain, as "Siffert lacks any example that shows an enhanced NHE-1 activity in patients with type II diabetes mellitus." *Id.* at 12.

These arguments are not persuasive. As the Examiner explains, "[t]he metric is whether or not the prior art would have made the administration of the instantly claimed composition to the instantly claimed patient population obvious, which it does, and the β-cell modulation mechanism would have followed." Ans. 9. Appellants' distinctions among the types and stages of diabetes, functional mechanisms, and treatment targets (*see, e.g.*, Appeal Br. 5–6, 8–10; Reply Br. 3–4) do not undercut this basic point. Although β-cell dysfunction does not characterize *all* stages or types of diabetes,[8] β-cell dysfunction was known to characterize, in particular, type II diabetes. This is sufficient to support the Examiner's rejection, in which Gericke's express

[8] The articles included by Appellants in the Evidence Appendix, which we have considered, amply demonstrate this point.

inclusion of "diabetes" among various therapeutic uses for rimeporide is supported by explanation of the link between type II diabetes and β-cell dysfunction in Tracey and Patti, as discussed above. *Cf. KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007) (observing that the ordinarily skilled artisan is "a person of ordinary creativity, not an automaton"). As for Siffert, Appellants' discussion (*see* Appeal Br. 12–14; *see also* Reply Br. 6–7) is directed largely to points for which the Examiner does not rely on Siffert. For this reason, the Examiner correctly observes that "[o]ne cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references." Ans. 21 (citing *In re Keller*, 642 F.2d 413 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091 (Fed. Cir. 1986)).

Appellants also argue that the Examiner's rejection misapplies the doctrine of inherency.[9] Appeal Br. 8; *see also* Reply Br. 4–5. In the context of obviousness, a disclosure is inherent if it is "sufficient to show that *the*

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[9] Appellants suggest inherency is limited to circumstances in which "a reference discloses **an actual embodiment** which meets all of the explicit steps of a method claim." Appeal Br. 7. This conception of inherency is under-inclusive, and, as the Examiner points out (*see* Ans. 13), is more descriptive of anticipation than obviousness. *In re Rijckaert*, 9 F.3d 1531 (Fed. Cir. 1993), on which Appellants rely (*see* Appeal Br. 7) distinguishes between optimal and inherent conditions, emphasizing that what "*may*" result is not sufficient for inherency. *Rijckaert*, 9 F.3d at 1534 (quoting *Oelrich*, 666 F.2d at 581–82). *Rijckaert* reaffirms the proposition that "[o]bviousness cannot be predicated on what is unknown," *id.* (quoting *In re Spormann*, 363 F.2d 444, 448 (CCPA 1966)), but cannot be interpreted as restrictively as Appellants suggest. In any event, the Examiner's rejection is not "predicated on what [was] unknown," for the reasons discussed above.

*natural result flowing* from the operation as taught would result in the performance of the questioned function." *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014) (quoting *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981)). Thus it has long been recognized that "the application of an old process to a new and analogous purpose does not involve invention, even if the new result had not before been contemplated." *Id.* (quoting *Ansonia Brass & Copper Co. v. Elec. Supply Co.*, 144 U.S. 11, 18 (1892)). Here, as the Examiner puts it, "it would have been obvious to administer rimeporide to patients with type II diabetes regardless of the instantly claimed inherent properties, and the inherent mechanism of action would have then necessarily followed." Ans. 12–13. "[E]fficacy is inherent in carrying out the claim steps." *In re Montgomery*, 677 F.3d 1375, 1381 (Fed. Cir. 2012). We discern no error in the Examiner's inherency analysis.

Having reviewed all of Appellants' arguments as presented in the Appeal Brief and further discussed in the Reply Brief, we are unpersuaded that the Examiner erred in rejecting claims 8, 14–16, 18, 20, and 24, for the reasons of record and as further explained herein.

*B. Claim 14*

Claim 14 depends from claim 8, and further recites "wherein the method is for treating Type II diabetes mellitus." Appeal Br. 17 (Claims Appendix). Referencing their previously-stated arguments, Appellants maintain that "none of the cited references teach the treatment specifically of type II diabetes with rimeporide." *Id.* at 14. This line of reasoning is unpersuasive for the same reasons as discussed above with respect to claims

8, 14–16, 18, 20, and 24, as the combination of references is sufficiently specific with respect to type II diabetes.

*C. Claims 22 and 23*

Claim 22 depends from claim 8, and further recites "wherein the pancreatic β-cell compensation in the patient is preserved to at least 70% of baseline prior to usage." Appeal Br. 17 (Claims Appendix). Claim 23 depends on claim 22, and further recites administration of rimeporide "for a period of at least 4 weeks." *Id.* Appellants argue that "[n]one of the prior art documents teach or suggest the administration of rimeporide for a period of 4 weeks with the result of decreasing β-cell dysfunction in the patient," and further that "none of the cited references teach the resulting significant advantageous effects found by appellants of preserving β-cell compensation to 70%." *Id.* at 14–15. The Examiner's optimization analysis, Appellants contend, fails because "the references provide no teaching regarding the effect on beta-cell dysfunction," and so "they obviously could not suggest optimizing their methods" as recited in claims 22 and 23. *Id.* at 15.

As discussed above, we agree with the Examiner that β-cell modulation would have been a natural consequence of what was suggested by the combined prior art, i.e., administering rimeporide to treat diabetes. Accordingly, we discern no error in the Examiner's finding that "dosing is a result determinate variable, and one of ordinary skill would have optimized the dose and regimen of 2-methyl-4,5-di-(methylsulfonyl)-benzoyl-guanidine for optimum efficacy in treating type II diabetes" based on the prior art teachings. Final Action 9. Further, Appellants do not appear to dispute (*see* Appeal Br. 14–15; Reply Br. 7) the Examiner's finding (*see*

Final Action 7–8 (citing Tracey ¶ 193)) that the prior art teaches a treatment regimen lasting six weeks. Thus, "the skilled artisan would have found it obvious to administer the rimeporide for greater than 4 weeks, which would have necessarily resulted in [] β-cell compensation to 70%." Ans. 24.

## CONCLUSION

The rejection of claims 8, 14–16, 18, 20, 22–24, 26, and 28 is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

## AFFIRMED